

1. A method for identifying a modulator of the enzymatic production of  $\beta$ -amyloid peptide ( $A\beta$ ) from  $\beta$ -amyloid precursor protein (APP) or a fragment thereof, comprising:  
providing a APP protease and BACE2 to a sample containing APP or an APP fragment;  
contacting the APP or the APP fragment and BACE2 with a candidate compound;  
and  
monitoring the effect of the candidate compound on the production of  $A\beta$ .
2. The method of claim 1, wherein said modulator is an inhibitor of  $A\beta$  production.
3. The method of claim 1, wherein the APP protease is a protease with  $\alpha$ -secretase activity.
4. The method of claim 1, wherein the APP protease is a protease with a  $\gamma$ -secretase activity.
5. The method of claim 1, wherein the APP protease is a protease with a  $\beta$ -secretase activity other than BACE2.
6. The method of claim 5, wherein said  $\beta$ -secretase activity is due to the presence of an enzyme having a pH optimum at about pH 6.5-7.0, and an estimated molecular weight of about 32-39 kDa as calculated from radiation inactivation analysis of HEK293 cell membrane extracts, or about 20-26 kDa as calculated from radiation inactivation analysis of human brain samples, with a candidate compound.
7. The method of claim 5, wherein said  $\beta$ -secretase activity is due to the presence of a  $\beta$ -secretase enzyme having a pH optimum at about pH 4.5-5.0 and an estimated molecular weight of about 50-60 kDa as calculated from radiation inactivation analysis of HEK293 cell membrane extracts or human brain samples (BACE1).
8. The method of claim 1, wherein the effect of the candidate compound on the production of  $A\beta$  is monitored by measuring the amount of  $A\beta$  formed.



9. The method of claim 8, wherein the amount of A $\beta$  formed is reduced by at least about 50%.
10. The method of claim 8, wherein the amount of A $\beta$  formed is reduced by at least about 75%.
11. The method of claim 8, wherein the amount of A $\beta$  formed is reduced by at least about 90%.
12. The method of claim 1, further comprising the step of comparing the effect of the test compound on A $\beta$  production with the effect of BACE2 in the absence of the test compound.
13. The method of claim 12, wherein the test compound causes at least about 15% reduction in the amount of A $\beta$  over the effect of BACE2 in the absence of the test compound.
14. The method of claim 13, wherein said reduction is at least about 25%.
15. The method of claim 13, wherein said reduction is at least about 50%.
16. The method of claim 13, wherein said reduction is at least about 75%.
17. The method of claim 1, further comprising the step of comparing the effect of the test compound on A $\beta$  production with A $\beta$  production in the absence of BACE2.
18. The method of claim 1, which is performed in a cell-free format.
19. A method for reducing the amount of  $\beta$ -amyloid deposits in the central nervous system (CNS) of a mammal comprising administering to said mammal an effective amount of BACE2 or an agonist thereof.
20. The method of claim 19 wherein said mammal is human.